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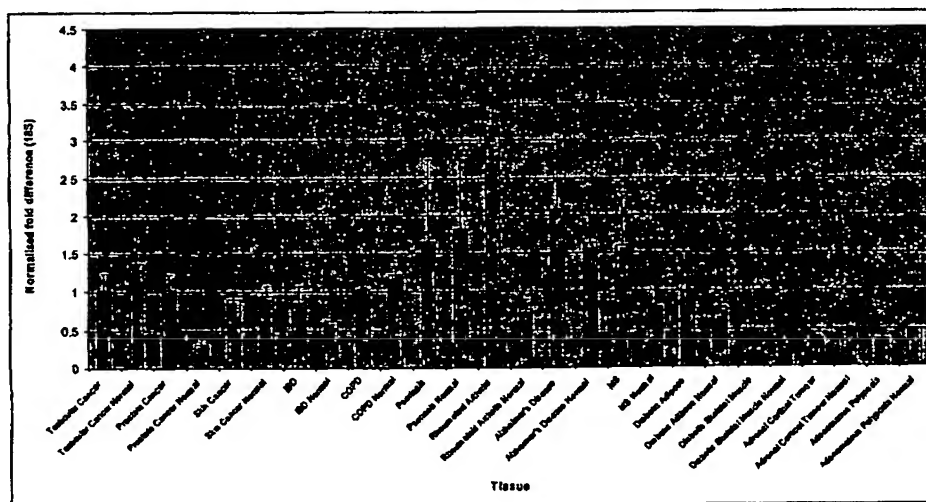
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MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC,
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ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,

[Continued on next page]

(54) Title: HUMAN NUCLEAR HORMONE RECEPTOR



(57) Abstract: This invention relates to the protein, termed BAB13403.1, herein identified as containing a Nuclear Hormone Receptor Ligand Binding Domain and to the use of this protein and nucleic acid sequence from the encoding gene in the diagnosis, prevention and treatment of disease.

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PCT/GB 03/02848

A. CLASSIFICATION OF SUBJECT MATTER

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G01N33/50 C12N5/10 A61K38/17 A61K39/00 A01K67/027

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C07K C12Q G01N A61K A01K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, SEQUENCE SEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NAGASE, T. ET AL.: "Prediction of the Coding Sequences of Unidentified Human Genes. XVIII. The Complete Sequences of 100 New cDNA Clones from Brain Which Code for Large Proteins in vitro" DNA RESEARCH, vol. 7, no. 4, 31 August 2000 (2000-08-31), pages 273-281, XP001012454 clone ID: KIAA1577 the whole document see especially: page 274; figure 1 page 275; table 1 and page 280; figure 3	1,7-15, 19-24, 28,32-45
X	-& DATABASE NCBI PROTEIN DATABASE [Online] 22 February 2001 (2001-02-22) NAGASE, T. ET AL.: "KIAA1577 protein [Homo -/--	1,7-15, 19-24, 28,32-45

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "A" document member of the same patent family

Date of the actual completion of the international search

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Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	sapiens]" Database accession no. BAB13403 XP002268259 cited in the application the whole document	
X	EGEA, P.F. ET AL.: "Crystal structure of the human RXRalpha ligand-binding domain bound to its natural ligand: 9-cis retinoic acid" EMBO JOURNAL, vol. 19, no. 11, 1 June 2000 (2000-06-01), pages 2592-2601, XP002268433 the whole document	1,6, 8-15, 19-24, 28-30, 32-45
X	WO 00 58473 A (CURAGEN CORPORATION) 5 October 2000 (2000-10-05) ORF ID: 2031 the whole document see especially: page 262; table 1 page 410; table 2 page 411; table 2 page 414; table 2 page 420; table 2 page 3248 -page 3249 SEQ ID NOS: 4061 and 4062 and page 5503 -page 5507; claims 1-32	1,7-15, 19-24, 28,32-45
L	DATABASE EMBL [Online] 20 January 2003 (2003-01-20) "Human polynucleotide SEQ ID NO: 648" Database accession no. ABZ11766 XP002268260 the whole document cited to provide information on the relevant sequence disclosed in W002070539 -& WO 02 070539 A (HYSEQ, INC.) 12 September 2002 (2002-09-12)	
P,X	SEQ ID NO: 648 the whole document see especially: page 107; table 1 page 111; table 1 page 114; table 1 page 120; table 1 page 1002; table 8 and page 1008 -page 1011; claims 1-27 --- -/--	1,7-15, 19-24, 28,32-45

INTERNATIONAL SEARCH REPORT

Intel Publication No
PCT/GB 03/02848

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
L	<p>DATABASE EMBL [Online] 20 January 2003 (2003-01-20) "Human polypeptide SEQ ID NO: 1596" Database accession no. ABP69549 XP002268261 the whole document cited to provide information on the relevant sequence disclosed in W002070539 - & WO 02 070539 A (HYSEQ, INC.) 12 September 2002 (2002-09-12)</p> <p>SEQ ID NO: 1596 the whole document see especially: page 208; table 2 page 1002; table 8 and page 1008 -page 1011; claims 1-27</p>	1,7-15, 19-24, 28,32-45
P,X		
X	<p>DATABASE EMBL [Online] 11 September 1997 (1997-09-11) NCI-CGAP: "n150d03.s1 NCI CGAP: Pr4 Homo sapiens cDNA clone IMAGE: 1044101, mRNA sequence" Database accession no. AA558357 XP002268262 derived from prostatic intraepithelial neoplasia - high grade the whole document</p>	1,7-15, 19-24, 28,32-45
X	<p>DATABASE EMBL [Online] 18 April 1997 (1997-04-18) ADAMS, M.D. ET AL.: "EST96990 Testis I Homo sapiens cDNA 5' end" Database accession no. AA383339 XP002268263 derived from testis the whole document</p>	1,7-15, 19-24, 28,32-45
A	<p>EGEA, P.F. ET AL.: "Molecular Recognition of Agonist Ligands by RXRs" MOLECULAR ENDOCRINOLOGY, vol. 16, no. 5, May 2002 (2002-05), pages 987-997, XP002268434 the whole document see especially: page 988, column 1, line 44 - line 50</p>	1-15, 19-24, 28-45

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 03/02848

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 35-37 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Although claims 20, 22-24, 28 and 38 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.2

Claims Nos.: 14, 19, 22, 28, 32, 34-37 (all partially) and 16-18, 25-27 (all completely)

Present claims 14, 19, 22, 28, 32 and 34-37 relate to a ligand defined by reference to a desirable characteristic or property, namely "which binds specifically to, and which preferably inhibits the nuclear hormone receptor ligand binding domain activity of a polypeptide according to any one of claims 1-7".

The claims cover all ligands having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such ligands. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the ligand by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the antibody as a ligand specifically binding and preferably inhibiting the nuclear hormone receptor ligand binding domain activity of a polypeptide according to claims 1-7 as claimed in claim 15.

Further, present claims 16-18 relate to a compound defined by reference to a desirable characteristic or property, namely "that either increases or decreases the level of expression or activity of a polypeptide according to any one of claims 1-7".

The claims cover all compounds having this characteristic or property, whereas the application provides no support within the meaning of Article 6 PCT and/or no disclosure within the meaning of Article 5 PCT for such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search impossible. Consequently, no search has been carried out for claims 16-18 and the search for the dependent

INTERNATIONAL SEARCH REPORT

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

claims 19, 32 and 34-37 has been restricted accordingly.

Moreover, present claims 25-27 relate to a method of diagnosing a disease in a patient involving a mutation defined by reference to a desirable characteristic or property, namely "which is associated with disease".

The claims cover all mutations having this characteristic or property, whereas the application provides no support within the meaning of Article 6 PCT and/or no disclosure within the meaning of Article 5 PCT for such mutations. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the mutation by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search impossible. Consequently, no search has been carried out for claims 25-27 and the search for the dependent claim 28 has been restricted accordingly.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Publication No

PCT/GB 03/02848

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0058473	A	05-10-2000	AU 3774500 A	16-10-2000
			CA 2383592 A1	05-10-2000
			EP 1165784 A2	02-01-2002
			WO 0058473 A2	05-10-2000
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			EP 1381621 A2	21-01-2004
			WO 02070539 A2	12-09-2002
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